Abstract ID: 17286 Title: Ultrasound Symposium: Computational modeling of high-intensity focused ultrasound mediated drug deliveryPurpose: Low-Temperature Sensitive Liposomes (LTSL) are drug delivery vehicles with that release the drug upon heating above ~40 ºC. The combination of LTSL with local heat generated by focused ultrasound may thus allow non-invasively targeted drug delivery. The complex interplay between heat based cancer treatments like thermal ablation and chemotherapy requires computational models to identify the relationship between heat exposure and pharmacokinetics in order to optimize drug delivery.

Methods: We developed mathematical models combining a model of tissue heating with a drug delivery model. Deposited HIFU energy (i.e. SAR) was calculated from phantom experiments, and used as input data for the model. Microvascular perfusion was modeled according to Pennes' Bioheat Equation, and was varied with temperature. A spatio-temporal multi-compartment pharmacokinetic model was created to describe the release of doxorubicin (DOX) from LTSL into the tumor plasma, subsequent transport into the interstitium, and finally uptake by the cells. Tissue was heated for varying times to target temperatures between 42 ºC and 60 ºC at the ultrasound focal spot, and spatio-temporal drug concentration profiles were calculated.

Results: At target temperatures in the hyperthermic range, maximum drug concentrations of ~ 9 ug/g were observed in the central heating area, with very localized drug deposition. At ablative temperatures similar maximum drug concentrations were observed, with a ring-like spatial concentration profile due to progressive shut-down of perfusion at temperatures above 45 ºC. Concentration increased approximately linearly with time during the examined time periods.

Conclusion: HIFU mediated targeted drug delivery via LTSL locally keeps plasma concentration of bioavailable drug high during hyperthermic temperature exposure, allowing for localized cellular uptake at heated locations. Heating induced temperature changes in perfusion considerably affect drug delivery, particularly if cessation of perfusion is induced. Multi-physics mathematical models may allow for optimization of heat-mediated targeted drug delivery from LTSL, as well as for treatment planning.

Educational objectives:
-Learn basic components of a drug delivery model
-Learn how computational models allow optimization of drug delivery
-Learn importance of treatment planning in targeted drug delivery